EFFECT OF ALUMINUM, CADMIUM AND LEAD ON RAT LUNG: PROTECTIVE ROLE OF SELENIUM.

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ABSTRACT

Adult male and female albino rats were treated orally with either sublethal doses of aluminum chloride, cadmium chloride or lead acetate alone or in combination with sublethal dose of sodium selenite. The rats were treated on alternate day for eight weeks and divided into eight groups of 5 rats each**:** control, (aluminum chloride 30 mg/kg bw, cadmium chloride 10 mg/kg bw and lead acetate 25 mg/kg bw) alone or in-combination with 0.4 mg/kg bw sodium selenite for each group. All animals were decapitated and lung tissues were dissected out, from each animal. Tissue samples were processed for light microscopical examination. Results showed that treatment with metals alone reduced rat body weight gain, and few rats died. There were many histopathological changes in the lung tissue of rats treated with metals alone such as, general impairment of the normal architectural organization of lung lobes and shredding of the bronchiolar epithelium cell with debris within its lumen and thickening of the interalveolar septa due to the inflammatory cells infiltrated of the alveolar walls. In some examined sections interalveolar septa ruptured forming large alveolar sacs as well as, hemorrhage and thick walled congested blood vessels. Many extrinsic allergic aveolitis were also seen in different areas of the pulmonary tissue. In some slides a lung abscess was seen and represented with a necrotic area and many pus cells. Administration of selenium concurrently with these metals ameliorated all the above adverse effects. In conclusion, Se has beneficial effects and could be able to antagonize Al, Cd and Pb toxicity on lung; effects that might be attributed to its antioxidant activity leading to scavenging free radicals.

***Keywords*:** Heavy metals; Cadmium chloride, Lead acetate, and Aluminum chloride, Antioxidants; Sodium selenite, lung rats.

INTRODUCTION

Aluminum, cadmium and lead are natural components of the Earth's crust. They can not be degraded and accumulate in living system through active circulation by food chain and in animal body and can be stored in soft (e.g. lung) and hard tissues (e.g. bones). They are taken into animal body via inhalation, ingestion and skin absorption **(Merian, 1991; Appleton *et al*., 2000)**.

Aluminum (Al) accumulation in animals can occur via the diet, drinking water, vaccines, antacids, parenteral fluids and inhaled fumes. Presently, Al utensils are widely used in the world especially in the developing countries, this may increase the Al content particularly in the food that are salty acidic or alkaline. Aluminum accumulation has been associated with a variety of human pathologies such as anemia, joint diseases, muscular weakness and Alzheimer's diseases **(Mohamed and Awad, 2008)**.

Cadmium (Cd) is a highly toxic element that is naturally present in all parts of the environment, including food, water, and soil **(Sherlock, 1984)**. Cadmium found in tobacco smoke, combustion of fossil fuels, industrial sources such as batteries, electroplatings, paints and fertilizers, pigments, metal coatings, plastics and some metal alloys **(Page *et al*., 1986; Bokori *et al*., 1996; Hart, 2000)**. It is also present in cigarette smoke, representing a significant source of exposure **(Stohs *et al*., 1997)**. Cadmium accumulates and proves to cause severe damage to a variety of organs such as lung, brain, testis, kidney, liver, blood system and bone **(Manca *et al*., 1991; Ercal *et al*., 2001)**.

Lead (Pb) is a natural element and widespread in the environment. This heavy metal is still mined and added to many products including paints, eye cosmetics, gasoline, water pipes and health care supplies. It depresses children's performances in intelligence and other functions **(Ashour *et al*., 2007)**.

Selenium (Se) is an essential element for humans and animals due to its antioxidant role and it is reported that Se has antagonistic effects against metal toxicity **(Burk, 2002)**.

The reported LD_{50} value in rats for aluminum chloride is 380-400 mg/kg bw **(Krasovskii *et al*., 1979)**, for cadmium chloride is 88 mg/kg bw **(USAF, 1990)**, for lead acetate is 4665 mg/kg bw **(Subranamoorthy and Baddaloo, 1995)** and for sodium selenite is 7 mg/kg bw **(Budavain *et al*., 1996)**.

Human exposure to these metals has risen dramatically in recent years due to excessive use of metals in industrial processes and products. Therefore, the present investigation was attempted to study the toxic effects of these metals especially the morphological alterations caused by them in rat lungs and the importance of antioxidants such as selenium in protecting living organisms against their the toxic effects.

MATERIALS AND METHODS

Chemicals:

Aluminum Chloride ($AlCl_3.6H_2O$, M. W. 241.43, Purity 99%), Cadmium Chloride ($CdCl_2.H_2O$, M. W. 183.32, Purity 99%), Lead Acetate [$((CH_3COO)2Pb.3H_2O$, M. W. 379.33, purity 99%)] and Sodium Selenite (Na_2O_3Se, M. W. 172.95, Purity 99.5%) were purchased from Electro Scient Chemicals Company, Kasr El-Eieny, Cairo.

Animals:

Adult male and virgin female albino rats ***(Rattus norvegicus albinus***) were purchased from Helwan farm of Egyptian Organization for Vaccine and Biological Preparations, Helwan, Egypt. Male and female rats were separated, maintained on ***ad Libitum*** diet and water and kept in an air-conditioned room (28 ± 2^oC) with a 12hr - light/dark cycle. The diet consisted of commercial brand of rabbit ration in pellet form containing all the dietary needs. It was obtained from El-Salam Factory for Dry Ration, EI-Marg, Cairo. All animals were housed in stainless steel cages (65 x 25 x 15 cm) with wire mesh bottom to minimize coprophagy as far as possible. All animals were healthy and clinically free from diseases.

Treatment Section:

A total of 40 adult males and 40 adult females with body weight ranging from 170-185 g for males and from 150 -170 g for females were allotted to groups. The first group **(Gr I)** received distilled water and served as control group. The second group **(Gr II)** was treated with sodium selenite alone. The third group **(Gr III)** was treated with the metal compound alone. The fourth group **(Gr IV)** was treated with a combination of metal

compound + sodium selenite. Prior to dosing, animals were deprived of food for 15-18 h overnight but given free access to water. Solutions of Al chloride, Cd chloride, Pb acetate and sodium selenite were dissolved in distilled water to prepare the appropriate stock solution for each. Hamilton syringe with blunt pointed needle was used for treated rats orally at a rate of 0.2 ml of each solution per 100 g rat bw. The selected sublethal doses were 0.4, 10, 25 and 30 mg/kg bw for sodium selenite, Cd chloride, lead acetate and Al chloride, respectively which represent 5.7%, 11.4%, 0.5% and 7.7% of their LD_{50} values, respectively. The selection of these sublethal doses was based upon either the results of our preliminary experiments or was in the neighborhood of those reported previously **(Jamba *et al*., 1997; Gupta *et al*., 1998; El-Demerdash *et al*., 2004; Al-Hashem *et al*., 2009)**. Animals were treated orally with these sublethal doses of metals alone or in combination with Se on alternate day for 8 weeks and the individual dosage was based on the most recently recorded body weight to provide the correct dose. During the experimentation period, body weight, signs of intoxication and death occurrence were recorded.

Histopathological Section:

At the end of the experiments (after 8 weeks), all numbers of males and females from the forementioned groups were sacrificed and their paired lungs were dissected out, trimmed of excess fat and weighted. These organs were prepared for histopathological examination according to **Pearse (1968)**.

Statistical Analysis of Data:

Data were statistically analyzed using computerized Instat prism 4 program. Data were presented as means ± SEM analyzed statistically using one way-ANOVA test followed by Tukey-Kramer multiple comparison post-test at $P \leq 0.05$ (n = 5).

RESULTS AND DISCUSSION

Aluminum chloride, cadmium chloride and lead acetate as metals and sodium selenite as an antioxidant were selected for the present study. Sublethal dose of each metal which represents approximately 5.7%, 11.4%, 0.5% and 7.7% of the LD_{50} values of Al chloride, Cd chloride, Pb acetate and sodium selenite, respectively were chosen. Adult male and female rats were treated orally with these sublethal doses on alternate day during the experimentation period of 8 weeks.

After 8 weeks from toxicant administration, rats were sacrificed for histopathological studies as well as measuring the relative weight of lung organ in relation to controls.

During the first half of experimentation period, rats exposed to sublethal doses of Al chloride, Cd chloride and Pb acetate did not show any signs of intoxication. The only conspicuous feature of intoxication was the reduction of their body weight gain compared to control rats. Data of **Fig. 1** showed that, regardless rat sex, the average body weight gain of rats treated with any metal alone **(Gr III)** increased gradually to reach the maximum value during the forth to the sixth week, then declined till the end of experimentation period. At that time (i.e. last three weeks) rats of **Gr III** of each metal became sluggish, showed uncontrolled urination and diarrhea and few rats died. For example, rats treated with sublethal doses of either Al chloride or Pb acetate caused death of one male rat during the 7^{th} week from metal administration, while rats treated with Cd chloride caused death of two animals of each sex during the 6^{th} week of Cd chloride administration. Accordingly, these results indicated that male rats are more susceptible to the candidate metals than females. The same trend was observed for rats subjected to treatments of **Fig. 1 E, F** and **Fig. 1 C, D** which females gained more weight than male rats.

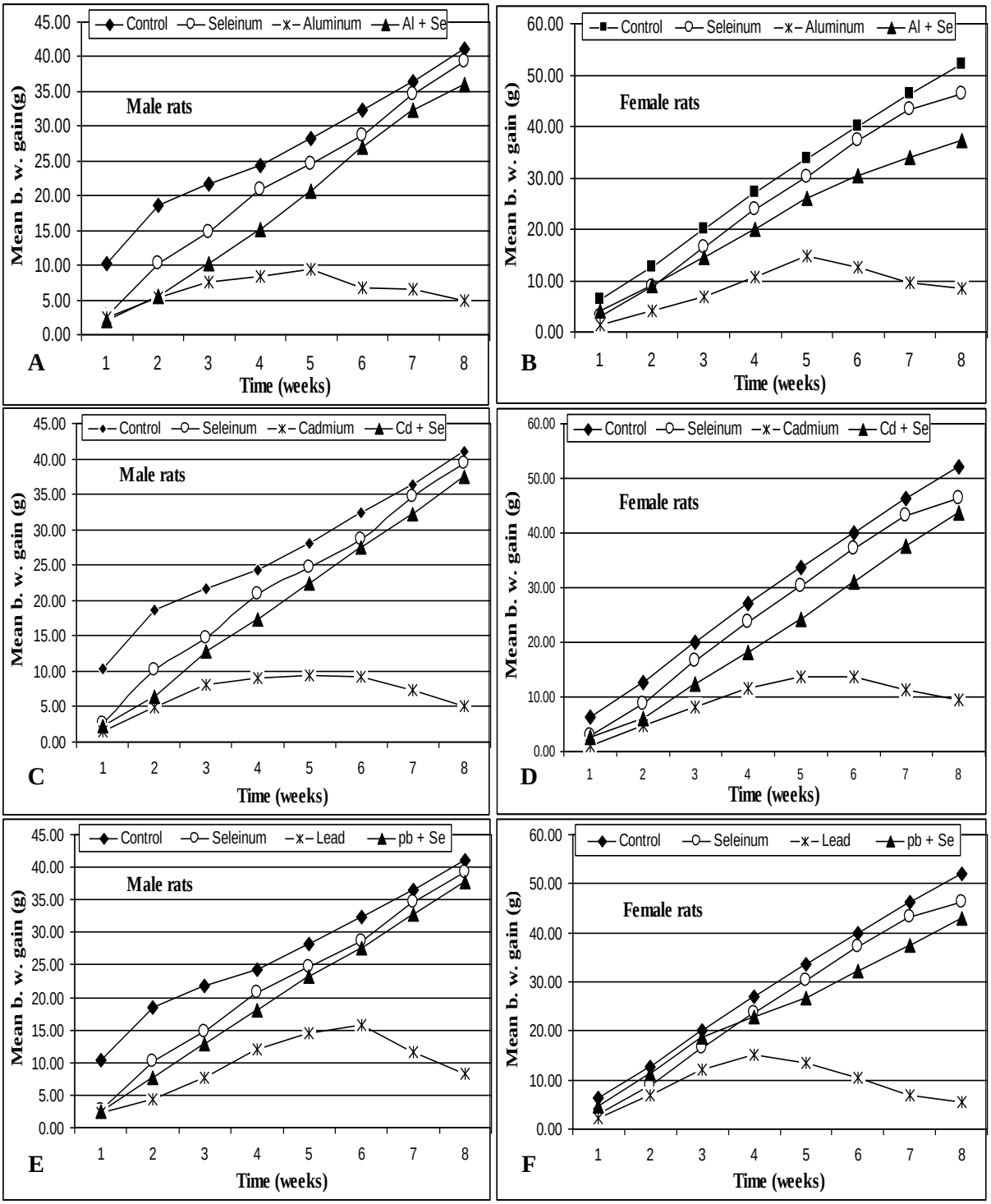

Fig. (1): Average weekly body weight gain (g) from initial body weights for control and treated adult male and female rats with Al, Se and Al + Se (**A, B**), Cd, Se and Cd + Se (**C, D**), pb, Se and pb + Se (**E, F**).

On the other hand, rats of **Gr I, II** and **IV** seemed to be healthy, their body weight gain increased significantly with time and all of them survived the treatments. The decreasing order of

body weight gain of experimental rats was as follows**:** rats of **Gr I > Gr II > Gr IV » Gr III** and that was true for all the candidate metals (**Fig. 1**). Data listed in this Figure revealed significant decrease in body weight of rats treated with each metal alone **(Gr III)** while highly significant improvement was recorded in rats treated with that metal + Se (i.e. corresponding **Gr IV)**.

The obtained results indicated that all the candidate metals showed delayed toxicity on adult rats **(Gr III)** as all of their adverse effects (i.e. severe reductions in body weight gain, manifestation of toxic symptoms and death occurrence) which took place during the last three weeks of experimentation period.

Teo *et al*. (2002) reported that reductions in body weight were sensitive indices of toxicity after exposure to toxic substances. Current results are in line with those obtained previously. For example, **Hammond and Beliles (1975)** reported that signs and symptoms of Cd toxicity were delayed some time after Cd administration. **Paternain *et al*. (1988)** found that rats treated orally with Al nitrate nonahydrate showed reduced food intake and subsequently they lost weight. **Mohamed *et al*. (1991)** cited that Cd exposure to rats resulted in reduced their body weight gain as well as decreased their spontaneous locomotor activities. **Alhazza (1999)** found that the body weight gain of rats treated with Pb acetate was less than that of control rats. He suggested that the growth depression was due to depression of appetite rather than reduced release of growth hormone or thyroxine. **Kjalf *et al*. (2001a)** postulated that the significant reduction on body weights of Cd treated animals might be attributed to severe alterations induced in different tissues due to Cd toxicity. **Baydar *et al*. (2003)** showed that treatment of rats with Al chloride caused considerable decrease in body weight gain from the first week of treatment and lasted throughout the experimentation period (8 weeks). They added that decreased body weight gain might indicate an adverse effect of Al on general health status which resulted from interference of Al with hormonal status and/or protein synthesis. Moreover, **Gong *et al*. (2005)** found that rats treated with Al chloride for 5 months showed increased escape latency due to brain dysfunction.

Data of **Fig. 1** indicated that administration of Se in association with each metal **(Gr IV)** improved rat's body weights significantly and gave remarkable protection against metal-intoxication. This piece of result is in accordance with those obtained previously (**Kjalf *et al*., 2001a; Yuan and Tang, 2001; El-Demerdash, 2004)**.

Lung Weight

The effects of the candidate metals on the relative weights of lungs of male and female rats after 8 weeks of treatments are shown in Table (١).

Data of Table (١) indicated that when any metal administered alone it caused a significant increase in the relative weights of lungs compared to those of control group. However, there were no significant differences in the relative weights of the lungs among rats treated with Al, Cd and Pb which indicated that the effects of the candidate metals on lung were approximately equal.

Data of Table (١) showed that there were no significant differences in the relative weights of all the examined lungs among rats treated with Se (**Gr II**), treated with the metal + Se (**Gr IV**) and control group (**Gr I**) which indicated that Se gave protection of these lungs against metal intoxication.

Lung is target organ following Cd exposure, with the severity of their intoxication dependent on the route, dose, and duration of the exposure to the metal. In the cell, Cd mainly accumulates in the cytosol (70 %), followed by the nucleus (15 %) and lowest in mitochondria and the endoplasmic reticulum **(Ognjanović *et al*., 1995; Štajn *et al*., 1997)**.

The finding that administration of any metal for a long time caused an increase in the relative weights of lungs are in accordance with those obtained previously **(Singh *et al*., 1976;**

El-Demerdash *et al*., 2004; Colomina *et al*., 1998). For example, **Singh *et al*. (1976)** suggested that the increased weight of lungs of lead-treated rats was, in part, due to lead accumulation in these organs.

Drill (1952) reported that when animals were administered the toxic agent, the enlargement of the lung was attributed to the accumulation of abnormal amount of fat in the parenchymal cells of treated rats. The acceptable explanation for the enlargement of lung was reported by **Fallon (1987)** who proposed that the lung most commonly injured by environmental chemicals during absorption, detoxification and excretion of chemicals.

Therefore, the enlargement of lungs is due to their increased activities. **ACP (1989)** stated that when rats were administered the toxic agent for a long time, it caused an increase in lungs weight possibly because lungs became swallon due to the presence of fluid in the trachea.

Table (١): Relative lung weight of rats treated orally with sublethal doses of Al, Cd and Pb with or without sodium selenite after 8 weeks.

Treatments		Sex	Relative weight
Gr I	Control	♂	0.88±0.005
		♀	0.81±0.005
Gr II	Se	♂	0.88±0.004
		♀	0.82±0.005
Gr III	Al	♂	2.46±0.094[a, c]
		♀	2.32±0.005[b, d]
	Cd	♂	2.40±0.007[a, c]
		♀	2.37±0.007[b, d]
	Pb	♂	2.37±0.007[a, c]
		♀	2.33±0.003[b, d]
Gr IV	Al + Se	♂	0.90±0.007[e]
		♀	0.88±0.005[f]
	Cd + Se	♂	0.92±0.005[e]
		♀	0.87±0.004[f]
	Pb + Se	♂	0.88±0.007[e]
		♀	0.83±0.005[f]

a: Significantly different from control male; **b:** Significantly different from control female; **c:** Significantly different from Se in male; **d:** Significantly different from Se in female; **e:** Significantly different from Al, Cd or Pb in male; **f:** Significantly different from Al, Cd or Pb in female using one way-ANOVA, followed by Tukey-Kramer for multiple comparison between groups.

$$\text{Relative lung weight} = \frac{\text{Absolute lung weight}}{\text{Whole body weight}} \times 100$$

Values are presented as means ± SEM (number of rats/group = 5).

Histopathological Changes

The effects of each metal administered alone or in combination with selenium on the histopathology of rat's lungs were examined in relation to those of control rats.

The histopathological examinations of all the specimens collected (The more apparent pictures were presented). The photomicrographs (**A**) presents a section in control lung. The photomicrographs (**B**) presents a section of intoxicated organ with a metal and the photomicrographs (**C**) presents a section in that organ when selenium was co-administered with that metal.

The histology of the normal lung is composed of thin-walled alveoli. The alveoli are composed of a single layer of squamous epithelium. Between the alveoli a thin layer of connective tissue and numerous capillaries also lined with simple squamous epithelium. Bronchioles can be recognized by the fact that they are lined by ciliated columnar epithelium (larger bronchioles) or by cuboidal epithelium (smaller bronchioles leading to alveoli) **(Fig. 2 A, 3 A and 4 A)**.

Our results showed that metals induced many histopathological changes in the lung of rats. General impairment of the normal architectural organization of lung lobes and shredding of the bronchiolar epithelium with cell with debris within its lumen and thickening of the interalveolar septa due to the inflammatory cells infiltrated of the alveolar walls. In some examined sections interalveolar septa ruptured forming large alveolar sacs as well as, hemorrhage, relative fatty change (represented with fat vacuoles) and thick walled congested blood vessel. Many extrinsic allergic alveolitis can also be seen in different areas of the pulmonary tissue. In some slides a lung abscess can be seen and represented with a necrotic area, large alveolus, macrophage, obstructed bronchus, enlarged and congested blood vessel and many pus cells within the lung tissue due to metals administration were noticed in **Fig 2 B, 3 B and 4 B**.

Lead binds to sulfhydryl groups intracellularly and interferes with numerous cellular enzymes, including those involved in heme synthesis. This binding accounts for the presence of lead in hair and nails. Lead also binds to mitochondrial membranes and interferes with protein and nucleic acid synthesis. **(Gerson, 1990; Greenberg, 1990; Hymphreys, 1991; Schraishuhn *et al*., 1992)**.

In the present study, rat lungs exposed to metals especially the interalveolar septa, contained mononuclear cell accumulation. As a result of cell invasion, the interalveolar septa were thickened, the alveolar surface became smaller and the alveoli were irregularly organized. Mononuclear cell invasion seen in the interalveolar septa can be described especially by macrophage and lymphocyte accumulation.

It has been reported that the thickness of the interalveolar septa not only depends on cellular origin but also on collagen fiber accumulation and capillary changes **(Peáo *et al*., 1994)**. The present study also identified collagen fiber accumulation along with inflammatory cell invasion in the interalveolar septa, effects which have been suggested by previous studies of lung morphology following lead exposure.

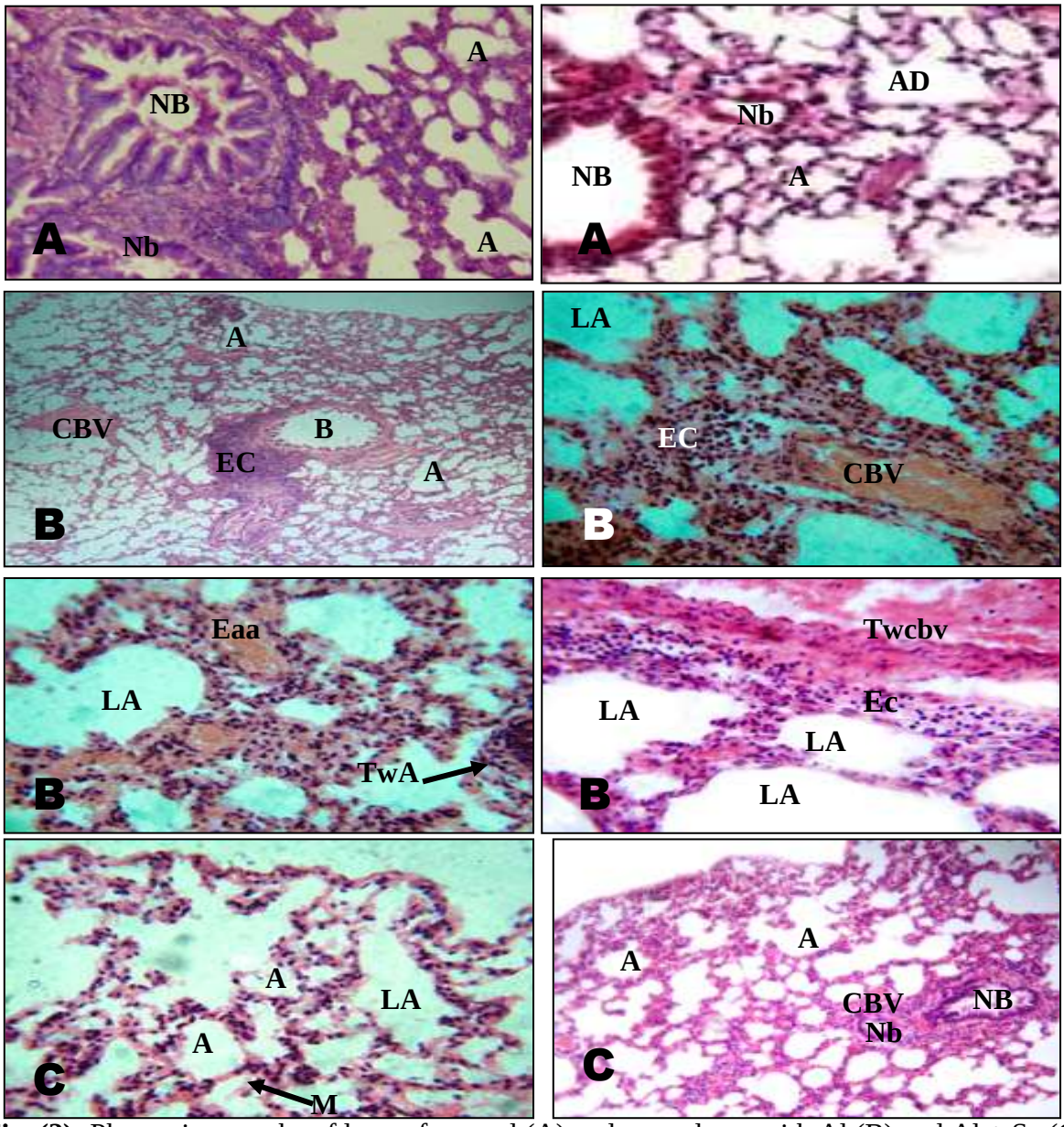

Fig. (2): Photomicrographs of lung of control (A) and treated rats with Al (B) and Al + Se (C).

(A) Section in control lung showing**:** Normal larger bronchioles (**NB**), smaller bronchioles (**Nb**), alveolar duct (**AD**) and alveoli (**A**). **(H/E x 400).**

(B) Section of intoxicated lung with aluminum chloride showing**:** Endothelial cells (**Ec**), Congested blood vessel **(CBV**), Thick walled congested blood vessels (**Twcbv**), Extrinsic allergic alveolitis **(Eaa**), Haemorrhage **(H**), Large Alveolus **(LA),** Thick Walled Alveolus **(TwA)**. **(H/E x 400)**.

(C) Section of treated lung with Al + Se showing**:** no significant alterations seen in comparison with control normal bronchioles (**NB**), smaller bronchioles (**Nb**), alveolar duct (**AD**) and alveoli (**A**), Endothelial cells (**Ec**), Congested blood vessel **(CBV**), Large Alveolus **(LA),** Macrophage **(M)**. **(H/E x 400).**

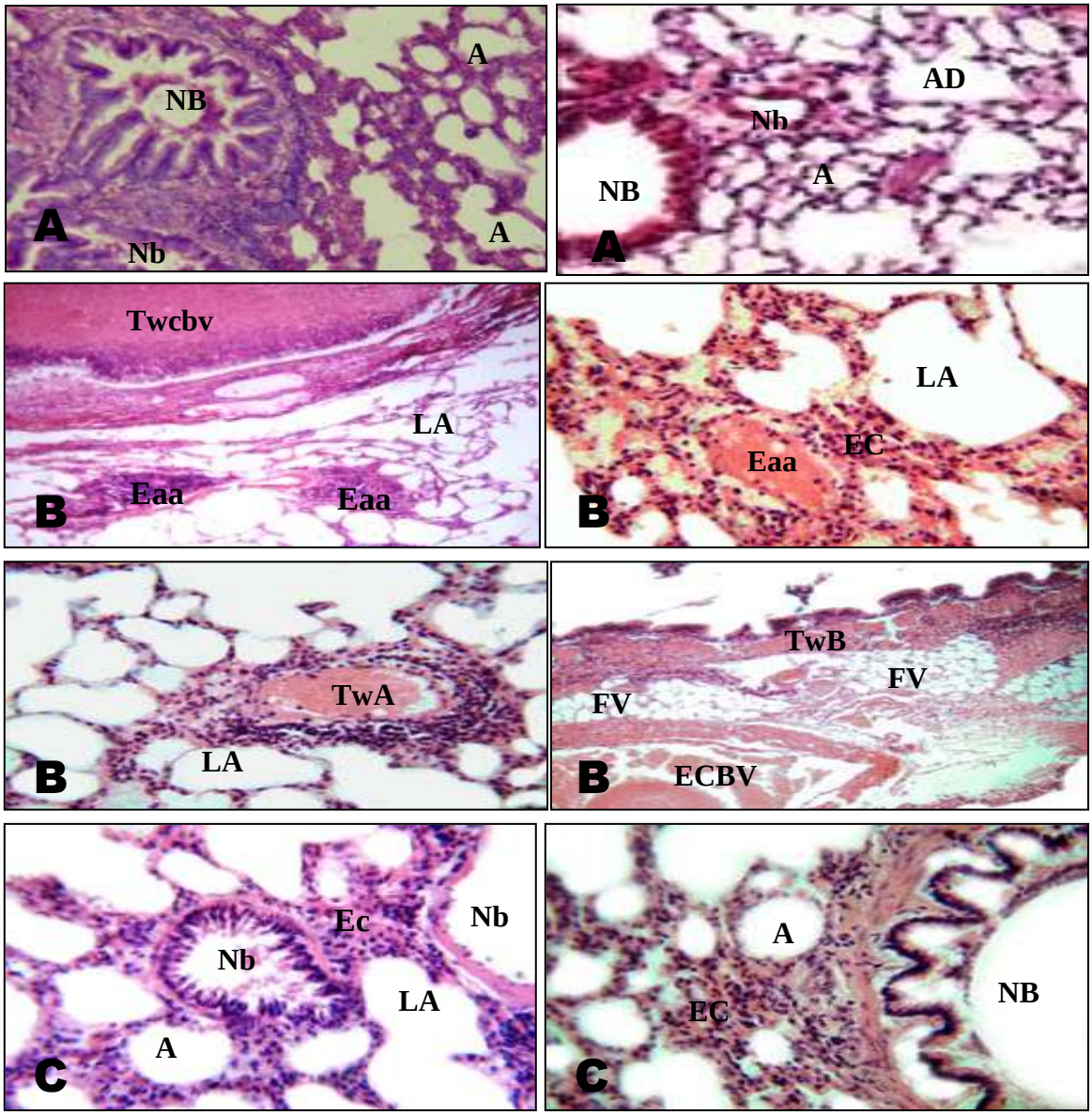

Fig. (3): Photomicrographs of lung control (A) and treated rats with Cd (B) and Cd + Se (C).

(A) Section in control lung showing**:** Normal larger bronchioles (**NB**), smaller bronchioles (**Nb**), alveolar duct (**AD**) and alveoli (**A**). **(H/E x 400).**

(B) Section of intoxicated lung with cadmium chloride showing**:** Endothelial cells (**Ec**), Congested blood vessel **(CBV**), Thick walled congested blood vessels (**Twcbv**), Extrinsic allergic alveolitis **(Eaa**), Thick Walled Alveolus **(TwA)**, Thick Walled Bronchus **(TwB),** Enlarged and Congested Blood Vessel **(ECBV),** Fat Vacuoles **(FV),** Large Alveolus **(LA)**. **(H/E x 400).**

(C) Section of treated lung with Cd + Se showing**:** no significant alterations seen in comparison with control normal larger bronchioles (**NB**), smaller bronchioles (**Nb**), alveolar duct (**AD**) and alveoli (**A**), Endothelial cells (**Ec**), Congested blood vessel **(CBV**), Large Alveolus **(LA)**. **(H/E x 400).**

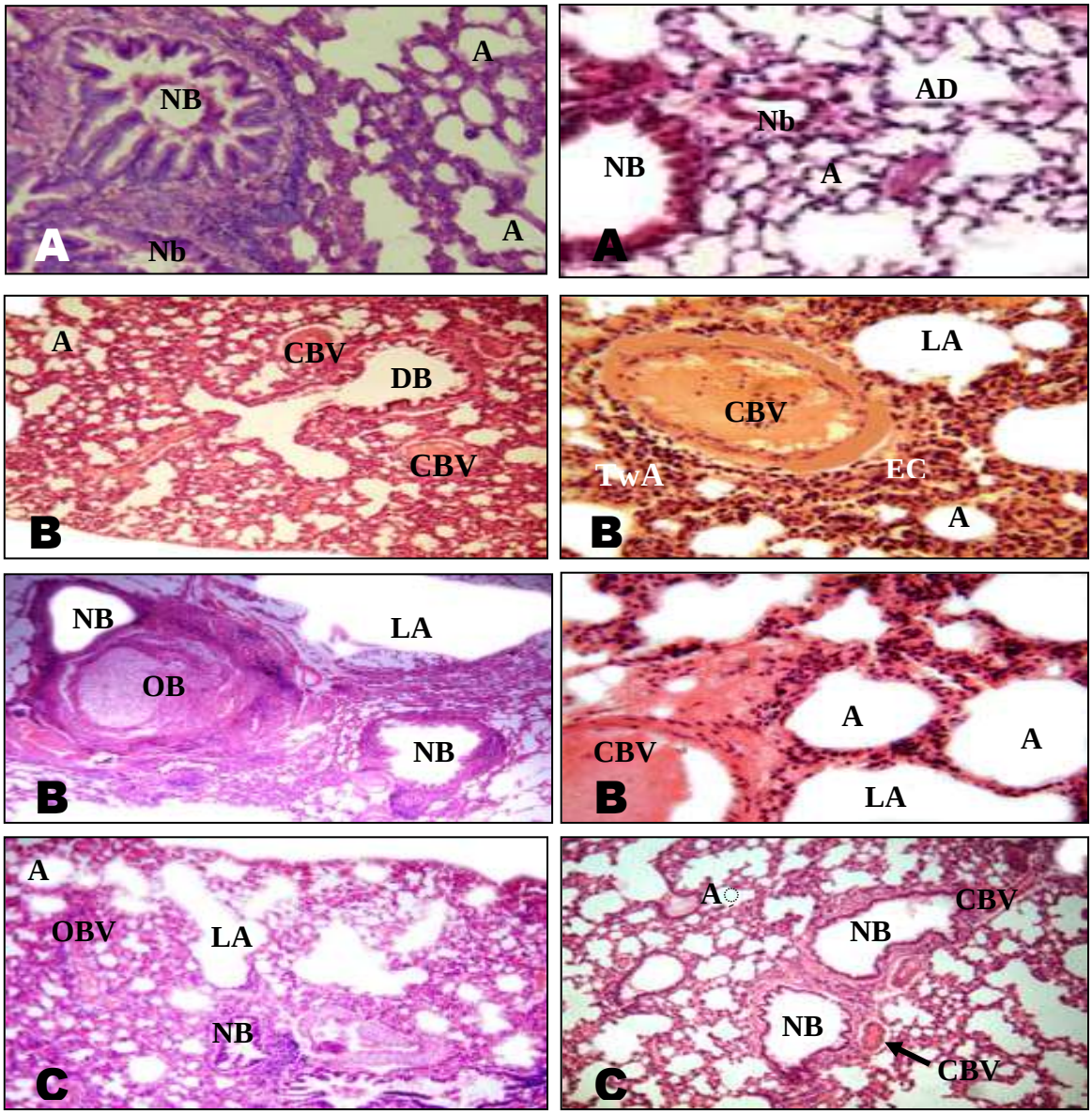

Fig (4): Photomicrographs of lung control (A) and treated rats with Pb (B) and Pb + Se (C).

(A) Section in control lung showing**:** Normal larger bronchioles (**NB**), smaller bronchioles (**Nb**), alveolar duct (**AD**) and alveoli (**A**). **(H/E x 400).**

(B) Section of intoxicated lung with lead acetate showing**:** Endothelial cells (**Ec**), Congested blood vessel **(CBV**), Extrinsic allergic alveolitis **(Eaa**), Large Alveolus **(LA)**, Obstructed Bronchus **(OB),** Thick Walled Alveolus **(TwA)**. **(H/E x 400).**

(C) Section of treated lung with Pb + Se showing**:** no significant alterations seen in comparison with control normal larger bronchioles (**NB**), smaller bronchioles (**Nb**), alveolar duct (**AD**) and alveoli (**A**), Endothelial cells (**Ec**), Congested blood vessel **(CBV**), Extrinsic allergic alveolitis **(Eaa**), Oedema blood vessel (**OBV**), Large Alveolus **(LA)**. **(H/E x 400).**

Previous pathological studies of heavy metal poisoning from cobalt, carbide, titanium, tantalum, lead, cadmium and aluminum have suggested fibrosis along with hyperplastic alveolar epithelium in the lung tissue, as well as asthma and pneumonia **(Haslam *et al*., 1980)**.

Chronic exposure to cadmium has been suspected as a cause of emphysema, obstructive lung disease, pulmonary fibrosis, and lung cancer **(El-Sokkary and Awadalla, 2011)**.

The morphological investigations of the current study revealed different changes in the lungs. Lung lesions are consisting of vascular severe inflammation in both alveoli and bronchioles with edema and congestion. These pathological changes are in agreement with the findings of **Shin *et al.* (2004)** who reported that the lung is a primary target organ of systemic exposure to cadmium. Because cadmium is mainly absorbed through the inhalation of industrial pollution and tobacco smoke, the result is the accumulation of this metal in the lung. Also, **Yamada *et al.* (1992)** noticed a dramatic increase in the number of alveolar neutrophilic leukocytes 6-48 h after exposure to cadmium chloride into lungs of dogs. **Bell *et al.* (2000)** reported that Cd exposure was deleterious to the lung tissue causing mild to severe inflammation in the lung. However, Cd has been implicated in the development of emphysema and pulmonary fibrosis **(Driscoll *et al*., 1992)**.

Mckenna *et al.* (1997) reported that Cd-exposed lungs showed acute and more chronic pulmonary inflammation in both rats and mice with bronchiolar and alveolar lesions.

Lung sections of treated rats with metals + Se showed relatively improvement of the lung tissues. Alveolar ducts, alveoli, blood vessels, bronchioles were nearly similar to that found in the lung of the control group, but there was thickening of the bronchiolar epithelium with cell debris intra its lumen in some areas of the lung tissue. Moderate congested blood vessels and infiltration of endothelial cells were also seen as in **Fig. 2 C, 3 C and 4 C**.

The histopathological examination obtained from the current study showed that metals have more damaging effects on lungs, which support the data listed in **Table (1)** in which male rats are more vulnerable to metal-intoxication than females.

The results indicated that selenium supplementation ameliorated to a large extent the lungs damages induced by the metal. These results are in accordance with those obtained previously **(Kjalf *et al*., 2001a; Kantola *et al*., 2004; Kara *et al*., 2007)**.

By reviewing the literature, it is clear that the mechanism of metal-toxicity is not fully understood. Therefore, the interpretation of its toxicity has been subjected to wide speculations by many investigators. Metal-toxicity might result from an alteration in lipid metabolism **(Petering *et al*., 1984)**. Others showed that metals caused oxidative damage in different tissues either by increasing lipid peroxidation of all cellular components or by inhibiting or decreasing the activities of the antioxidant enzymes (e.g. glutathion peroxidase, catalase, superoxide dismutase …..etc.) either by replacing their metal cofactor or binding with-SH group of proteins **(El-Demerdash *et al*., 2004; El-Sharaky *et al*., 2007; Soliman, 2008)**. Accordingly, metal can cause loss in the ability of cell membrane to act as a barrier (i.e. it destroys cell membrane integrity) leading to the loss of catalytic enzymes and substrates from intracellular stores. This speculation is the key factor in producing injury in lung following metal exposure **(Hussain *et al*., 1987)**. It is believed that metals interfere with element homeostasis in animal body and that could play an important role in their toxicity **(Faurskov and Bjerregaad, 1997)**.

On the other hand, selenium is known to have antagonistic effects against metal toxicity, although the precise mechanism is not known. One possible mechanism is the formation of a chemical complex between Se and metal which reduces the availability of free metal-ions in the body, by this way prevents its interference with various chemical functions **(Badiello *et al*., 1996)**. The more acceptable mechanism is its alleviation of oxidative stress caused by metal, either by scavenging the oxidative free radicals or by increasing the activities of antioxidant enzymes. Thus, Se can maintain cell membrane integrity which protects cellular components to interact with these free radicals **(Stajn *et al*., 1997; Kantola *et al*., 2004; Kara *et al*., 2007)**.

Se has a certain protective role from the toxic actions of heavy metals **(Jamall and Sprowls, 1987; Ognjanovic *et al*., 1995; Zikic *et al*., 1998)**. This protection includes the capability of Se to alter the distribution of metals in tissues and induces binding of the metal-Se complexes to proteins, which are similar to metallothioneins (**Jamba *et al*., 1997; Combs and Gray, 1998)**.

CONCLUSION:

Aluminum, cadmium and lead have adverse effects on human health. The present study demonstrated that selenium administered in combination with Al, Cd or Pb minimized their hazards. Therefore, it would seem wise to administer antioxidants (e.g. vitamins or selenium) as crucial defense mechanism against metals-induced toxicity through scavenging free radicals.

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التأثير الضار لكل من الألومنيوم ، الكادميوم والرصاص علي رئة الجرذان البيضاء ودور السيلينيوم في الحماية.

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أجريت هذه الدراسة لإختبار التأثيرات الضاره لكل من الألومنيوم ، الكادميوم والرصاص علي التركيب التشريحي للرئة لذكور وإناث الفئران البيضاء ودور عنصر السيلينيوم في الحماية من هذه التأثيرات وتم ذلك بتعريض هذه الفئران لجرعة غير مميتة يوم بعد يوم لمدة ٨ أسابيع بجرعات **٣٠، ١٠، ٢٥** مجم/كجم من وزن الجسم من كلاً من كلوريد الألومنيوم و كلوريد الكادميوم وأسيتات الرصاص علي الترتيب بمفردها وأيضاً بخلطها بجرعة غير مميتة قدرها **٠.٤** مجم/كجم من وزن الجسم من عنصر السيلينيوم (سيلينات الصوديوم). وبعد إنتهاء فترة التجربة تم ذبح كل الفئران للحصول علي الرئة وأخذ الوزن الرطب لها وعمل قطاعات هستولوجية بها. وأشارت النتائج إلي أن معاملة الفئران بهذه المعادن أحدث إنخفاضاً ملحوظاً في أوزانها وتدهوراً في حالتها الصحية مع وجود بعض حالات الوفاة، كما حدثت زيادة في أوزان الرئة نتيجة لحدوث ضرر في هذه الأنسجة والذي يتمثل في حدوث النزيف وتحول دهني لنسيج الرئة في أماكن مختلفة كما لوحظ وجود إحتقان في الأوعية الدموية وموت لبعض الأنسجة وذلك مقارنةً بالفئران في المجموعة الضابطة. أما الفئران المعاملة بهذه المعادن مضافاً إليها عنصر السيلينيوم فكانت تتمتع بصحة جيدة مع زيادة أوزانها كما في المجموعة الضابطة ، بالإضافة إلي عدم تأثر نسيج الرئة الخاص بها وذلك لأن عنصر السيلينيوم قام بحماية هذه الفئران من التأثيرات الضارة والمؤذية لهذه المعادن السامة.